RESEARCH ARTICLE

Mortality from Stomach Cancer in Serbia, Excluding the Province of Kosovo, in the 1991-2009 Period

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Abstract

Background/Aim: Stomach cancer is the second most common cause of death from all malignant tumors in the world (third in men, fifth in women), with a strong decreasing trend in most developed countries. The aim of this descriptive epidemiological study was to analyze mortality of stomach cancer in Serbia, excluding the Province of Kosovo, in the 1991-2009 period. Materials and Methods: In data analysis, we used mortality rates which were standardized directly using those of the world population as a standard. In order to analyze the mortality trend from stomach cancer, linear trend and regression analysis were used. Confidence intervals (CIs) for the average age-adjusted and age-specific mortality rates were assessed with 95% level of probability. Mortality data were derived from the data file of the Statistical Office of the Republic of Serbia. Results: During the 1991-2009 period, a significant downward trend in mortality of stomach cancer was recorded in Serbia (y=9.78 - 0.13x, p=0.000; average annual percent change was - 6.3 (95%CI, -7.8 to - 4.8). During the same period, a significant decrease in mortality trend was found both in male (y=14.13 - 0.20x; p=0.000; % change was -7.7 (95%CI, -10.9 to -4.5) and female populations (y=6.27 - 0.08x; p=0.000; % change was - 4.4 (95%CI, -5.3 to -3.6). Conclusion: Decreasing trends in mortality from stomach cancer in Serbia are similar to those in most developed countries.

Keywords: Stomach cancer - mortality - descriptive epidemiologic study

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Introduction

Malignant stomach tumors are the second leading cause of death among malignant tumors, with more than 730,000 deaths, accounting for 10% of total deaths worldwide in 2008 (Jemal et al., 2011). The highest stomach cancer mortality rates in 2008 were recorded in Asia (Mongolia - 26.5 per 100,000 inhabitants, China - 22,3 per 100,000 inhabitants, Bhutan - 22.1 per 100,000 inhabitants) (IARC, 2008). The lowest mortality rates were recorded in certain South African countries (Botswana - 0.3 per 100,000 inhabitants and Namibia - 1.1 per 100,000 inhabitants), and United States of America - 2.0 per 100,000 inhabitants. Over 75% of stomach cancer cases (556,471 cases) occur in developing countries (353,685 men vs. 202,786 women) (IARC, 2008; Jemal et al., 2011). Nearly 72% of deaths were recorded in Asia, almost 66.5% of which occurred in China.

Stomach cancer rates are about twice as high in males as in females (Parkin, 2004; Ferlay et al., 2010; Jemal et al., 2011). Stomach cancer mortality starts to rise in middle-aged adults of both genders (45-64 years of age), and becomes even more frequent in the elderly (75 years of age and above) (Look et al., 2001). The mortality of stomach cancer has decreased considerably in most developed countries over the past several decades (Levi et al., 2003). Similar trends, but with later onset, were also observed in some Asian countries, including Japan and China (Lee et al., 2006).

The aim of this descriptive epidemiological analysis was to estimate death rates for stomach cancer and their secular trends in the population of Serbia over the 1991-2009 period.

Materials and Methods

The mortality rates are calculated from data collected by the Statistical Office of the Republic of Serbia, which receives death certificates and compiles mortality data by gender, age, year, and cause of death. We used the International Classification of Diseases, 9th and 10th Revision, to classify codes of deaths (WHO). Data on the deceased from all causes of death were used in the study (codes 001-999 by 9th and A00-Z99 by 10th revision of the International Statistical Classification of Diseases, Injuries and Causes of Death), all malignant tumors (codes 140-209, 9th Revision and C00-C97, 10th Revision), symptoms, signs and abnormal clinical and laboratory findings (codes

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780-799, 9th Revision and R00-R99, 10th Revision), and malignant stomach tumors (code 151, 9th Revision and C16, 10th Revision). Population size and composition by age and gender were obtained from the 1991 and 2002 censuses.

Age-adjusted mortality rates were calculated by direct standardization, using the world standard population (Jensen et al, 1991). Cases were grouped by gender into 10-year age groups at diagnosis. Age-adjusted and age-specific mortality rates were calculated using midperiod population denominators for each age group. Linear trend model was used to examine trends of mortality from stomach cancer. An estimate of the linear trend in the age-adjusted stomach cancer mortality rates was obtained by fitting Poisson regression models to the data observed over the period 1991-2009, adjusting for the effects of age.

Percent changes of mortality rates were calculated as the percent difference between the adjusted rates of two successive years, and then as an average of these changes for the entire observation period. Confidence intervals (CIs) for the average age-adjusted and age-specific mortality rates were assessed with 95% level of probability.

Two-sided P values are reported and are considered to indicate statistical significance when they are less than 0.05. Data were processed using the Statistical Package for the Social Sciences, version 19.0 (SPSS Inc, Chicago, IL, USA).

Results

Over the 19-year observation period, in the Republic of Serbia, excluding the Province of Kosovo, a significant decrease in total mortality was observed (y=799.31-7.78x; p=0.000; % average annual percent change=- 0.10 (95%CI=-0.13 to -0.07)), with a significant increase in deaths from all malignant tumours (y=119.69+1.18x; p=0.000; %change=+0.82 (95%CI=0.74-0.90) (Figure 1). Mortality of stomach malignant tumours decreased (y=9.78-0.13x; p=0.000; %change= -6.3 (95%CI=-7.8 to -4.8). The non-significant downward trend (y=63.33-0.83x; p=0.151; % change=-0.14) was observed for mortality where causes of death were symptoms, signs and abnormal clinical and laboratory findings.

In the same period, mortality of stomach malignant tumours significantly decreased among males [y=14.13 - 0.20x; p=0.000; %change=-7.7 (95%CI=-10.9 to -4.5)], and females (y=6.27 - 0.08x; p=0.000; % change=- 4.4 (95%CI=-5.3 to -3.6)) (Figure 2). On average, men died of stomach malignant tumours 2.2 times more frequently than women.

Stomach cancer mortality rates increase with age and are the highest in people aged 70 and older (Table 1). Low mortality rates were recorded in both men and women aged under 45. In terms of gender, age-specific rates were notably higher among males than among females, and the differences were the highest for age 60-79. In the

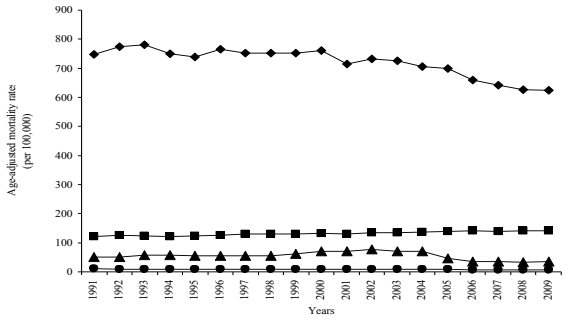

Figure 1. Trends in Age-Adjusted Mortality Rates for Choosen Causes in Serbia, Excluding the Province of Kosovo, in 1991-2009 Period. Rhombs - all causes; squares - all malignant tumours; triangles - symptoms, signs and abnormal clinical and laboratory findings; circles - stomach cancer

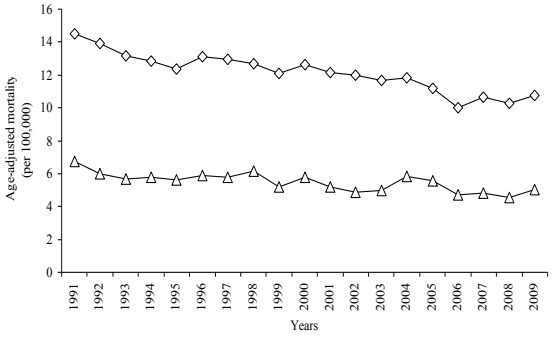

Figure 2. Trends in Age-Adjusted Mortality Rates for Stomach Cancer in Serbia, Excluding the Province of Kosovo, by Gender, in 1991-2009 Period. Rhombs - male; triangles - female

Table 1. Average Age-Specific Mortality rates and Linear Trend of Stomach Cancer in Serbia, Excluding the Province of Kosovo, by Gender, in 1991-2009 Period

Age	Male				Female			
	Age-specific rates* (per 100,000)	Linear trend	P	Average annual percent change (95%CI)	Age-specific rates* (per 100,000)	Linear trend	P	Average annual percent change (95%CI)
≤ 19	0.05	†			0.02	†		
20-29	0.34	y= 0.55-0.02x	0.017	- 13.6 (-24.5 to -2.8)	0.25	†		
30-39	1.82	y= 2.38-0.06x	0.049	- 3.7 (-7.4 to -0.01)	1.73	y= 2.36-0.06x	0.042	- 3.6 (-7.0 to -0.20)
40-49	8.54	y= 10.04-1.15x	0.001	- 3.3 (-5.0 to -1.60)	4.73	†		
50-59	25.64	y= 30.52-0.49x	0	- 1.3 (-1.8 to -0.90)	10.97	y=12.80-0.18x	0.018	- 1.6 (-2.8 to -0.30)
60-69	63.67	y= 76.08-1.24x	0	- 0.7 (-0.8 to -0.50)	25.43	y=28.80-0.34x	0.034	- 0.7 (-1.4 to -0.06)
70-79	113.23	y=126.57-1.33x	0.001	- 0.4 (-0.6 to -0.20)	49.59	y=57.35-0.78x	0.001	- 0.6 (-1.0 to -0.30)
80+	93.41	†			55.59	†		

*Average age-specific mortality rates (per 100,000) for stomach cancer in Serbia, excluding the Province of Kosovo, in 1991-2009 period; CI-Confidence Interval; †None of the regression analysis models corresponded to mortality data for this age group

observation period, a significant decrease in the rates of deaths caused by stomach cancer is recorded in men aged 20-29, 30-39, 40-49, 50-59, 60-69, 70-79. The female population also demonstrated a significant decrease in deaths caused by stomach cancer in age groups with middle-aged (30-39 years of age) and elderly women (50-59, 60-69, 70-79). None of the regression analysis models corresponded to mortality data for other age groups.

Discussion

In spite of the strong downward mortality rates worldwide, stomach cancer is the second most important cause of death from cancer worldwide (Parkin, 2004; Jemal et al., 2011). In Serbia, with 1313 deaths and 5.4% in total number of deaths from malignant tumors in 2008, stomach cancer takes the fourth place.

Stomach cancer mortality rates in different populations around the world vary by more than tenfold (IARC, 2008). Nearly three-fourths of stomach cancers occur in developing countries. Mortality rates in men and women in 2008 ranged from 20.3 per 100,000 people in East Asia to 2.1 per 100,000 in North America (IARC, 2008; Ferlay et al., 2010). The highest mortality rates were recorded in Asia (Mongolia -26.5 per 100,000) and parts of South America (Honduras -22.3 per 100,000, Peru 18.2, Chile -15.0) in men and women. In contrast, the lowest rates were observed in men and women in North America and most parts of Africa (approximately 2 per 100,000). Across Europe, major differences in stomach cancer death rates are evident (IARC, 2008). The stomach cancer rates in Russian Federation (15.2 per 100,000) are more than five times higher than those in Scandinavia or France (close to 3.0 per 100,000), and higher stomach cancer rates are generally observed in Eastern Europe (Kyrgyzstan -20.1, Belarus -18.8). Moderately high death rates of stomach cancer are observed in Bosnia and Herzegovina (7.7 per 100,000), Serbia (7.4), Italy (6.6), Spain (6.0), Greece (5.0), Finland (4.4). The lowest rates in Europe in 2008 are found in Cyprus (2.9 per 100,000), Switzerland (3.0), and Iceland, Sweden and France metropolitan (3.2 per 100,000 all).

Mortality rates in men are 2-3 times higher than in women. The highest mortality rates are estimated in Eastern Asia (28.1 per 100,000 in men, 13.0 per 100,000 in women), and the lowest in Northern America (2.8 and 1.5, respectively). High mortality rates are also present in both genders in Central and Eastern Europe, and in Central and South America (IARC, 2008; Jemal et al., 2011). Differences in stomach cancer mortality in men and women are associated with differences in incidence of various adenocarcinoma subtypes by histology (intestinal/diffuse) and location (proximal/distal) (Munoz et al., 1968; Ekström et al., 2000). Diffuse adenocarcinoma occur more frequently in women, while in men is dominant intestinal adenocarcinoma, the subtype being responsible for most of the international variations.

Stomach cancer is rare in children and young adults. In Serbia, as in most countries, stomach cancer mortality rates start to rise in middle-aged adults (45-64 years of age), and it is even more common in the elderly (75 years of age and older) age group for males and females, respectively (Howlader et al., 2011). In the second half of 20th century, stomach cancer mortality in Japan has reached the mortality levels in Western countries, which may be explained by introduction of stomach cancer screening in Japan and life style changes, including reduced salt intake and increased intake of fruit and vegetables, reduction in smoking and prevention of Helicobacter pylori infection (Inoue et al., 2005; Lee et al., 2006). In addition, studies of immigrants suggest significant reduction of stomach cancer risk in Japanese immigrants to the lower risk areas (Maskarinec et al., 2004), even though numerous results indicate the importance of exposure to enviromental factors during childhood in determining risk (Coggon et al., 1990).

In both men in women, in the past decades the stomach cancer mortality has been showing significant downward trend in most of the developed countries (Amiri et al., 2011; Howlader et al., 2011). Stomach cancer mortality rates declined between 1980 and 2005 at about the same rate (3.6-4.9% per year) for both men and women in seven European countries (Denmark, Finland, France metropolitan, the Netherlands, Norway, Sweden, and England and Wales) (Amiri et al., 2011). The US mortality trend for stomach cancer between 1990-2008, showed significant decrease for all races, with the average annual percent change -3.0% in both genders, and -3.4% in male and -2.7% in female (Howlader et al., 2011). Similar trend, but with later onset, was observed in Asian countries, including Japan and China (Lee et al., 2006; Yang, 2006).

The international variation in mortality, time trends, and the impact of migration on mortality from stomach cancer are mainly due to differences in socio-economic environment and lifestyle, education and health care system has begun in recent decades. Factors leading to the decrease in stomach cancer mortality include broader availability of fresh fruit and vegetables, less salt and conserved food in the diet, better food conservation including refrigeration, decreased incidence of chronic infections with *Helicobacter pylori* resulting from improved hygiene and use of antibiotics, and introduction of the screening program (Levi et al., 2004; Parkin, 2004; Lee et al., 2006; Yang, 2006). Evidence linking Helicobacter pylori infection with stomach cancer risk contributed to the 1994 International Agency for Research on Cancer's classification of the bacterium as carcinogenic to humans (IARC, 1994). International prevalence variations of Helicobacter pylori infection demonstrate certain similarities with those of the stomach cancer; in developing countries, prevalence of *Helicobacter pylori* infection in adults is estimated to 76% vs. 58% in developed countries. High prevalence of the Helicobacter pylori infection with minor international differences indicates that some other factors play significant role in the stomach cancer etiology (Parkin et al., 2002). While some authors (Ngoan et al., 2002; Ito et al., 2003) believe diet plays no role in the stomach cancer etiology, American Cancer Society lists smoked foods, salted fish and meats, and pickled vegetables as risk factors for stomach cancer (American Cancer Society, 2010). On the other hand, eating fresh fruits and vegetables that contain antioxidative

vitamins (such as vitamins A and C) lowers the risk of stomach cancer. In addition, a significant inverse correlation between Mediterranean diet and stomach cancer has been well-established (Munoz et al., 1997). The risk of stomach cancer is increased significantly by cigarette smoking (40% in smokers, and by 82% in heavy smokers) and alcohol intake (IARC, 2004). Some researchers have pointed out the correlation between lack or excess of iodine, goiter and stomach cancer, and reduced mortality from the stomach cancer following effective iodine prophylaxis (Gołkowski et al., 2007).

Although at different times and with different rates, mortality from stomach cancer shows a declining trend in developed countries. Even though statistically non-significant, downward mortality trend during 1991-2008 period in Serbia - where symptoms, signs and insufficiently defined conditions were specified as causes of death - indicates the necessity of cautious interpretation of mortality statistics in international comparisons. It is yet to be determined whether improved treatment has played a role in stomach cancer mortality trends in Serbia. There are limited data on stomach cancer risk factors in the Serbian population. Analytical epidemiological studies are required to determine whether the main risk factors for stomach cancer are frequent in the population of Serbia.

In conclusion, downward trends in mortality from stomach cancer in Serbia are similar to those in most developed countries. The next improvement in mortality trends can be achieved through primary prevention and screening of patients at particular risk of stomach cancer. Planning and evaluation activities for the management of stomach cancer requires analytical epidemiological studies.

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